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10/719,532	11/21/2003	David Follansbee	DAVFOL.002C1	3410

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	03/19/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 03/19/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/719,532	FOLLANSBEE, DAVID	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *7,9,10 and 13-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/21/2003 & 09/19/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24 are pending.

2. Applicant's election without traverse of Group I, Claims 1-6, 8 and 11-12, in the reply filed on 09/19/2006 and the species of Dicrocoelium dendriticum in the reply filed on 12/12//2006 are acknowledged.

3. Claims 7, 9-10 and 13-24 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

4. Claims 1-6, 8 and 11-12 are currently under examination as they read on a pharmaceutical composition comprising at least one helminth-based agent and a vaccine comprising the pharmaceutical composition.

5. Applicant's IDS filed on 11/21/2003 and 09/19/2006 are acknowledged.

Claim Objections

6. Claim 6 is objected to because of the following informalities: Claim 6 is dependent upon the formulation of claim 3, but recites the "the method of claim 3". Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 and the specification on pages 7, 20 and 31 the discloses the term 'dendtriticum.' The worm species of fluke disclosed is misspelled and should be Dicrocoelium 'dendriticum.'

Claim 8 recites "wherein said protein is a recombinant cell." A protein is not a cell, so this claims limitation is without meaning.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-6, 8 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention.

The specification does not provide reasonable enablement for: A pharmaceutical formulation for **preventing** or treating allergies or asthma in a mammal comprising **at least one helminth-based agent**, wherein said helminth-based agent is capable of ameliorating the allergic reaction **to a plurality of antigens** of claim 1; further comprising at least one pharmaceutically acceptable compound selected from the group consisting of one or more of the following: adjuvants, carriers and diluents of claim 2; wherein said helminth-based agent comprises an immunogenic amount of a helminthic antigen of claim 3; wherein said helminthic antigen is an isolated protein selected from the group consisting of one or more of the following: **nematodes, trematodes and cestodes** of claim 4; wherein said helminthic antigen **comprises a protein isolated from a helminth**, wherein said helminth is parasitic to humans of claim 5; wherein said **helminthic antigen comprises an isolated protein** selected from the group consisting of one or more of the following: Capillaria hepatica and Dicrocoelium dendtriticum of claim 6; wherein said helminth-based agent comprises **a protein** isolated from a helminth, wherein **said protein is a recombinant cell** transformed with a nucleic acid molecule encoding said protein of claim 8; wherein said pharmaceutical formulation comprises in a form selected from the group consisting of one or more of the following: injectable fluids, suppositories, powder, tablets, capsules, syrups, suspensions, liquids and elixirs of claim 11; or A **vaccine** for **preventing** allergies or

asthma in a mammal comprising the pharmaceutical formulation of claim 1 in an amount sufficient to regulate IgE of claim12.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has only disclosed the theoretical use of "antigenic material" and "antigenic protein" to invoke "the desired immune response" in Examples 1 and 2 (In particular, page 32). The specification is directed to the use of any helminthic agent given to any animal to reduce any allergy. On page 7, the helminthic antigen is preferably isolated from Capillaria hepatica and/or Dicrocoelium dendtritium and/or Schistosomes. However, there is no data to enable the claims.

The claims encompass the use of any helminthic "agent" comprising any helminthic protein or antigen from any nematode, trematode or cestode for use in preventing any allergy. But, the specification does not provide support commensurate in scope with the claim recitations. In addition, any helminthic agent as encompassed by the claims, such as a crude extract, will contain helminthic components that are not responsible for decreasing allergy and that may actually cause a separate inflammatory response or other undesirable side-effects.

Although the benefit of some helminths to downregulate allergic responses has been documented, Carvalho et al. (PTO-892, Page 2, Reference V) teaches that helminths synthesize protease molecules that provoke allergenic responses and that excretory/secretory products of helminths can actually induce Th2 responses. In addition, some helminthic antigens cross-react

with allergens which can increase allergic reaction in atopic individuals and initiate allergic diseases in non-atopic individuals (In particular, page 529, paragraph spanning left and right columns). Cooper et al. (PTO-892, Page 2, Reference W) teaches that geohelminthic parasites secrete potent allergens and can be capable of enhancing allergic inflammation as evidenced by asthmatic symptom decrease upon anti-helminthic treatments (In particular, page 399 second to last paragraph of left column). Further, Falcone et al. provides insight into the state of the art in disclosing that, as of 2005, clinical trials were ongoing (PTO-892, Page 2, Reference X). If positive immunosuppressive results are demonstrated, those parasites will be then mined for immuno-suppressive molecules that can be used in appropriate sustained-delivery formulations to mimic successful immunological responses induced by natural infections. (In particular, page 159, paragraph spanning left and right columns). Therefore, the art is highly unpredictable and it would require and undue amount of experimentation to practice the claimed invention.

The term "vaccine" recited in 12 implies complete prevention of disease. The specification fails to provide guidance as to how to totally prevent (100% prevention) allergy. Allergy is a very complex disease involving a large number of diverse antigens. The prevention of any and all allergic diseases and symptoms using any and all helminthic antigen preparations has not been adequately been disclosed in the specification. The specification also does not sufficiently enable the prevention of any specific allergy with any specific helminthic antigen.

There is a complete lack of guidance in the specification as to what helminths, helminth proteins or helminth antigens would be useful in the present invention. The lack of guidance

does not provide sufficient enablement of the claims because the art teaches that helminthic regulation of allergy is highly unpredictable. The claims encompass many helminth antigens that would not work. For example, the art in Wilson et al. (PTO-892, Page 3, Reference U) teaches that helminth-driven suppression of allergic inflammation is mediated by CD25+ upregulated T cells. However, expression of CD25 depends on both many defined and as-yet unknown factors (In particular, abstract, page 1203, 'Anti-CD25 antibodies block supression' section). Expression is associated with the induction of specific cytokines, namely IL-10 and TGF- β, but there is no evidence in the reference or otherwise that all helminth antigens upregulate CD25 on T cells. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

14. Claims 1-6, 8 and 11-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of: A pharmaceutical formulation for preventing or treating allergies or asthma in a mammal comprising **at least one helminth-based agent**, wherein said helminth-based agent is capable of ameliorating the allergic reaction **to a plurality of antigens** of claim 1; further comprising at least one pharmaceutically acceptable compound selected from the group consisting of one or more of the following: adjuvants, carriers and diluents of claim 2; wherein said helminth-based agent comprises an immunogenic amount of a helminthic antigen of claim 3; wherein said helminthic antigen is an isolated protein selected from the group consisting of one or more of the following: **nematodes, trematodes and cestodes** of claim 4; wherein said helminthic antigen **comprises a protein isolated from a helminth**, wherein said helminth is parasitic to humans of claim 5; wherein said **helminthic antigen comprises an isolated protein** selected from the group consisting of one or more of the following: Capillaria hepatica and Dicrocoelium dendtriticum of claim 6; wherein said helminth-based agent comprises **a protein** isolated from a helminth, wherein **said protein is a recombinant cell** transformed with a nucleic acid molecule encoding said protein of claim 8; wherein said pharmaceutical formulation comprises in a form selected from the group consisting of one or more of the following: injectable fluids, suppositories, powder, tablets, capsules, syrups, suspensions, liquids and elixirs of claim 11; or A vaccine for preventing allergies or asthma in a mammal comprising the pharmaceutical formulation of claim 1 in an amount sufficient to regulate IgE of claim12.

The claims encompass the use of any helminthic "agent" comprising any helminthic protein or antigen from any nematode, trematode or cestode for use in preventing any allergy. But, the specification does not provide support commensurate in scope with the claim recitations.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of helminthic species to describe the claimed genus, nor does it provide a description of structural features that are common to species of helminth-based agent, helminthic antigen or protein isolated from a helminth. The specification provides no description what helminths, helminthic proteins or helminthic antigens would work in the present invention; in essence, the specification simply directs those skilled in the art to go figure out for themselves what helminthic antigen preparations to use. The claims read on any as yet undiscovered helminths and helminthic proteins, antigens and molecules. Therefore, the specification's disclosure is inadequate to describe the claimed genus of an helminth-based agent, helminthic antigen.

Applicant has recited in the examples only "antigenic substance" and "antigenic protein" without reference to the use of any specific helminth or any specific helminth derived substance, protein or antigen. The skilled artisan cannot envision all the contemplated helminth derived agents recited in the instant claims. The specification has recited no structure for the claimed invention. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the

Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-5 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by De Macedo et al. (PTO-892, Reference U) as evidenced by PTO-892, Reference V.

De Macedo et al. teaches Ascaris suum (helminth, nematode) extract (helminth-based agent, protein) isolated from live Ascaris suspended in borate buffered saline (carrier/diluent) (In particular, page 702, section entitled 'Antigens). The antigen (helminthic antigen) was administered to mice (immunogenic amount) with ovalbumin (Oa); dinitrophenol ovalbumin (DNP-Oa); and/or aluminum hydroxide (adjuvant) by injection (injectable liquid, vaccine) (In particular, page 702, column spanning left and right columns). Reference V is being used as an evidentiary reference to show that Ascaris suum is an intestinal roundworm that is parasitic to humans.

A composition is a composition, regardless of its intended use. Therefore, the reference teachings anticipate the claimed invention.

13. Claims 1-5 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Ferreira et al. (PTO-892, Reference W) as evidenced by PTO-892, Reference V.

Ferreira teaches Ascaris suum (helminth, nematode) extract (helminth-based agent, protein, antigen, helminthic antigen) suspended in complete Freund's adjuvant administered to mice (immunogenic amount) with ovalbumin by injection (injectable liquid, vaccine) (In particular, pages 202-203, sections on 'Reagents, Antigens and Cell Line' and 'Immunization and Skin Testing'). Reference V is being used as an evidentiary reference to show that Ascaris suum is an intestinal roundworm that is parasitic to humans.

A composition is a composition, regardless of its intended use. Therefore, the reference teachings anticipate the claimed invention.

14. Claims 1-5, 8 and 11-12 are rejected under 102(a) as being anticipated by U.S. Patent 6,207, 158 (PTO-892, Reference X).

The '158 patent teaches the migration inhibitory factor protein (MIF) of the Dirofilaria immitis and Onchocerca vulvulus parasitic helminths (In particular, column, 3, lines 5-37) and use thereof in a vaccine. The reference also teaches recombinant cells that include the parasitic MIF nuclei acid molecules (In particular, column 3, lines 38-43). Onchocerca vulvulus causes river blindness in humans (In particular, column 2, lines 13-19) and Dirofilaria immitis causes heartworm infection in dogs and other animals including humans (In particular, column 2, lines 7-12). The compositions comprising the MIF protein are administered in an immunogenic amount (In particular, column 23, lines 31-50) with a variety of adjuvants and carriers (In

particular, column 22, lines 51 to column 23, line 3) in a variety of formulations (injectable fluids) (In particular, column 22, lines 31-50).

A composition is a composition, regardless of its intended use. Therefore, the reference teachings anticipate the claimed invention.

15. Claims 1-5, 8 and 11-12 are rejected under 102(b) as being anticipated by U.S. Patent 5,996,758 (IDS filed on 09/19/2006) as evidenced by (PTO-892, Reference X)

The '758 patent teaches cysteine protease, a secretory protein accumulated in the tissue of the Paragonimus westermani (Trematode) parasitic helminths. The protein ((helminth-based agent, helminth antigen, protein) is extracted and purified and put in a pharmaceutical composition with Freund's adjuvant and injected into rabbits (vaccine) (In particular, column 3, lines 32 to 48). Pharmaceutical compositions of helminthic cysteine protease can be in various forms including injectable solutions (In particular, column 10, lines 14 -20). The protein may also be produced recombinantly in cultured animal cells transformed with the nucleic acid (column 10, lines 25-31). Reference X is being supplied to show that Paragonimus westermani is a trematode that is parasitic to humans.

A composition is a composition, regardless of its intended use. Therefore, the reference teachings anticipate the claimed invention.

16. Claims 1-6 and 11-12 are rejected under 102(b) as being anticipated by Gonzalez-Lanza et al. (PTO-892, Page 2, Reference U).

Gonzalez-Lanza et al. teaches the whole-worm extract (helminth-based agent, helminthic antigen, protein) of adult D. dendriticum (In particular, page 473, 'Preparation of Antigens' section). The reference also teaches the preparation of ES antigen (helminth-based agent, helminthic antigen, protein) from D. dendriticum. Both whole-worm extract and ES antigen preparations were suspended in $NaHCO_3/NaCO_3$ (carrier/diluent).

A composition is a composition, regardless of its intended use. Therefore, the reference teachings anticipate the claimed invention.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free)

March 12, 2007

Nora M. Rooney, M.S., J.D.

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Maher M. Haddad

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